

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application.

1-20. (Cancelled)

21. (Previously presented) A method of manufacturing a bioprosthetic heart valve, comprising

(a) providing an acellular matrix,

(b) seeding said matrix with isolated myofibroblasts and isolated endothelial cells;

and

(c) culturing said myofibroblasts and said endothelial cells under pulsatile flow conditions;

thereby producing a cellularized bioprosthetic heart valve.

22. (Previously presented) The method of claim 21, wherein said myofibroblasts are derived from an intended recipient of said heart valve.

23. (Previously presented) The method of claim 21, wherein the acellular matrix is seeded with isolated myofibroblasts, isolated endothelial cells, and at least one other isolated cell type.

24. (Previously presented) The method of claim 23, wherein the other isolated cell type is secretory cell.

25. (Cancelled)

26. (Previously presented) The method of claim 21, wherein the culturing comprises culturing in tissue culture media consisting of at least one growth factor, or at least one cell signaling factor, or a combination of at least one growth factor and at least one cell signaling factor.

27. (Previously presented) The method of claim 26, wherein the tissue culture media comprises an endothelial cell-conditioned media.

28. (Previously presented) The method of claim 26, wherein said growth factor or said cell signaling factor is recombinant, synthetic or isolated from conditioned media.

29. (Previously presented) The method of claim 21, wherein the acellular matrix is chosen from the group consisting of an acellular valve structure, a decellularized valve structure or a synthetic valve structure.

30. (Previously presented) The method of claim 29, wherein the acellular matrix is a decellularized porcine valve.

31. (Previously presented) The method of claim 21, wherein the myofibroblasts are resistant to dedifferentiation.

32. (Previously presented) The method of claim 21, wherein the myofibroblasts are obtained from cardiac tissue, vascular tissue, or dermal tissue.

33. (Previously presented) The method of claim 32, wherein the cardiac tissue comprises mammalian heart leaflet interstitial tissue.

34. (Previously presented) The method of claim 32, wherein the dermal tissue is cultured under conditions that promote a myofibroblast-like phenotype.

35. (Previously presented) The method of claim 21, wherein the myofibroblasts are derived from a human donor.

36. (Previously presented) The method of claim 35, wherein the human donor is histocompatible.

37. (Previously presented) The method of claim 23, wherein the at least one other isolated cell type comprises cells derived from a human donor.

38. (Previously presented) The method of claim 37, wherein the human donor is histocompatible.

39. (Previously presented) The method of claim 21, wherein the myofibroblasts are syngeneic with respect to an intended recipient of the bioprosthetic valve.

40. (Previously presented) The method of claim 23, wherein the cells are syngeneic with respect to an intended recipient of the bioprosthetic valve.

41. (Previously presented) The method of claim 21, wherein the myofibroblasts are cultured in the presence of a purified or recombinant growth factor.

42. (Previously presented) The method of claim 21, wherein the myofibroblasts produce type I collagen.

43. (Previously presented) The method of claim 42, wherein the myofibroblasts produce at least two-fold more type I collagen compared to type III collagen.

44. (Previously presented) The method of claim 21, wherein the myofibroblasts are cultured under pulsatile flow conditions comprising flow values of 2-7.5 liters/min, a frequency of 60-120 cycles/min, and resistances to duplicate back pressures of up to 120 mm Hg.

45. (Previously presented) The method of claim 21, wherein the myofibroblasts comprise genetically-modified myofibroblasts.

46. (Previously presented) The method of claim 45, wherein the genetically modified myofibroblasts produce an increased level of collagen I, fibronectin, glycosaminoglycans, recombinant actin and myosin, or heparin, compared to a normal, untreated myofibroblast.

47. (Previously presented) The method of claim 45, wherein the genetically modified myofibroblasts express at least one recombinant polypeptide chosen from bFGF, VEGF, fibronectin, beta 1 integrin, TGF-beta-1, alpha 1 type I collagen, aortic-type smooth muscle alpha-actin, or myosin light chain 1.

48. (Previously presented) The method of claim 21, wherein at least 60% of the total collagen produced by said myofibroblasts is type I collagen.

49. (Previously presented) The method of claim 21, wherein less than 25% of the total collagen production by said myofibroblast is type III collagen.

50. (Previously presented) The method of claim 45, wherein myofibroblasts are genetically altered to increase type I collagen production relative to type III collagen production.

51. (Previously presented) The method of claim 21, wherein an external layer of said valve comprises a monolayer of said endothelial cells and wherein an inner layer comprises said isolated myofibroblasts.

52. (New) The method of claim 21, wherein the valve is human.